

DIJK et al
Appl. No. 10/587,525
November 4, 2010

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REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

The claims have been revised to define the invention with additional clarity. The claims as presented are supported by an enabling disclosure.

Claims 10-27 stand rejected under 35 USC 112, second paragraph, as allegedly being indefinite. Withdrawal of the rejection is submitted to be in order in view of the above-noted claim revisions and comments that follow.

Claim 10 has been revised to replace the word "providing" with the word "manufacturing". Basis for this amendment can be found, for example, at paragraph [0018], last full sentence, of US 2007/0160711.

As regards the Examiner's objection to the phrases "a more mature taste" and "increasing the flavor intensity", it will be clear from paragraphs [0018] and [0019] of the published application that the CPD-I treated cheese is compared to a control cheese, which control cheese was manufactured without the use of CPD-1. The claims have been amended to reflect this. Furthermore, it is clear from the last sentence of paragraph [0018] that sensory analysis was used to determine the effect of CPD-1. Sensory analysis was a well known technique for testing cheese (see, for example, Figure 1 of R1, cited by the Examiner). Attention is directed to the fact that comparable language (enhancing the flavour of a cheese) was used in R1.

The claims have been amended to make clear that the carboxypeptidase preparation and the carboxypeptidase activity refer to carboxypeptidase CPD-1.

In view of the above, reconsideration is requested.

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Claims 10-27 stand rejected under 35 USC 103 as allegedly being obvious over Yvon et al (referred to as R1) in view of Delest et al. (referred to as R2). Withdrawal of the rejection is submitted to be in order for the reasons that follow.

Example 1 of R1 is an "*in vitro*" test in which 4 of the 20 possible amino acids were tested. According to Example 1, the amino acids Tyrosine (Tyr, Y), Phenylalanine (Phe, F), Tryptophan (Trp, W) and Leucine (Leu, L) were increasingly catabolized by the tested micro-organism in the presence of a keto-acid. The other 16 amino acids were not tested. The relevance of the other amino acids in an "*in vitro*" assay is, therefore, not known. A question presented is whether these "*in vitro*" data reflect the situation in a real end application (such as cheese).

Example 2 involves a cheese (i.e., an "*in vivo*") test. In this Example, one amino acid (phenylalanine) of the 20 possible amino acids, was tested and it was concluded that, in the presence of alpha-ketoglutarate, more phenylalanine was degraded as compared to a situation in which no alpha-ketoglutarate was used. The other 19 amino acids were not tested. The relevance of the other amino acids in an "*in vivo*" assay is, therefore, not known.

Example 3 relates to an organoleptic test.

Example 4 involves another cheese test. In Table III of Example 4 it is shown that the amino acids Methionine (Met, M), Isoleucine (Ile, I), leucine, and phenylalanine seem to be important (see column 8, lines 60-63) and that Aspartate (Asp, D), Alanine (Ala, A), Valine (Val, V), tyrosine and orthinine could also have an effect (column 8, line 64). According to column 9, lines 9 and 10: "The other amino acids are in equivalent quantity in both cheeses." This means that, for example, tryptopan which was considered important in the "*in vitro*" results of Example 1 does not seem to be important under "*in vivo*" conditions. In other words, the results of Example 1 are not relevant to the claimed invention.

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In Example 5, tests were performed in liquid media ("*in vitro*"?) and pseudocurd ("*in vivo*"?). These tests relate to phenylalanine and leucine only.

Upon comparing the results of Examples 1 and 4, it is clear that there is no 100% correlation between the "*in vitro*" data of Example 1 and the "*in vivo*" data of Example 4. For example, tryptophan, which was considered important in Example 1, does not seem to be important in Example 4.

Column 8 of R2 shows multiple combinations of endo- and exoproteases:

- (a) streptogrisin B or trypsin or papain endoprotease with CPDII (to release Arg or Lys, i.e., R or K); R and K are according to Example 4 of R1, not relevant for the claimed subject matter.
- (b) chymotrypsin or thermolysin or neutral protease with CPDI (to release Tyr, Phe or Trp, i.e., Y, F or W); according to Example 4 of R1, W does not seem to be important and Y only to a lesser extent. Combination (b) has only one important amino acid (i.e., F) in common with Example 4 of R1.
- (c) Thermolysin or neutral protease with bacterial leucyl aminopeptidase or leucyl aminopeptidase from *Aspergillus* (to release Leu, Ile, Phe or Val, i.e., L, I, F or V). This combination has 3 amino acids (L, I and F) in common with the allegedly important amino acids of Example 4 of R1.
- (d) Neutral protease or subtilisin with CPD1 (to release Phe or Ala, i.e., F or A). This combination has 1 important and one less important amino acid in common with the identified amino acids of Example 4 of R1.

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- (e) Elastase with CPD I (to release Ala, i.e., A). This combination provides one of the amino acids which, according to Example 4 of R1, could also have an effect but does not seem to be a major amino acid.
- (f) Rennet-like proteases with leucyl aminopeptidase from *Aspergillus* or methionyl aminopeptidase (to release Met, i.e., M). This combination provides one of the amino acids which, according to Example 4 of R1, is allegedly important.
- (g) Engineered proline-specific peptidyl-prolyl cis trans isomerase (cypsoase) with prolyl amino peptidase (to release Pro, i.e., P); this amino acid is, according to Example 4 of R1, not relevant.
- (h) Proline-specific endoprotease with malt enzymes or CPD-Y (to release Pro, i.e., P); this amino acid is, according to Example 4 of R1, not relevant.
- (i) Glutamyl endopeptidase with CPD-1 (to release Glu, i.e., E) this amino acid is according to Example 4 of R1, not relevant.

From this analysis (and using the Examiner's approach) it is clear that only combination (c) would be considered in any way relevant to assessing obviousness. However, combination (c) would have pointed the skilled person to the use of bacterial leucyl aminopeptidase or leucyl aminopeptidase from *Aspergillus* and not to the use of CPD-1. Accordingly, the instant claims would not have been obvious over the combination of R1 and R2.

Furthermore, combinations (b), (d), (e) and (i) make clear that the effect (i.e., the release of specific amino acids) by CPD-1 depends heavily on the specific combination with the exemplified endoproteases. Only combinations (d) and (e) share one amino acid (alanine). All other predicted amino acids in the combinations (b), (d), (e) and (i) differ from each other. In other words, it would not have been predictable what the end result would have been if a

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combination of an endoprotease and CPD-I had been used, let alone what the result would have been if a combination of a coagulant (see point 13 on page 5 of the Office Action) and CPD-I had been used.

Finally, it is noted that the only combination that makes reference to a coagulant is combination (f) which refers to a rennet-like protease. If this combination were to have been considered, then the exoprotease suggested would have been a leucyl aminopeptidase from *Aspergillus* or methionyl aminopeptidase.


It will be clear from the foregoing that the present invention would not have been obvious over of R1 and R2. Reconsideration is requested.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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